Western Carolina University
Office of Research Administration
Institutional Review Board Standard Operating Procedures

SOP# 301.1	TITLE: Unanticipated Problems and Adverse Events	Date Effective: 01/01/2022 Last Revision Date: 06/30/2021

I. Purpose

This procedure sets forth the process for reporting, reviewing, and correcting unanticipated problems, protocol deviations, protocol violations and adverse events.

II. Definitions

Adverse Event is defined as an event either anticipated or unanticipated that result in direct or actual physical, psychological, economic, or social harm to the participants. Examples include the death of a research participant, a participant experiencing a negative reaction after participating in the research intervention, a change made to the research protocol to immediately eliminate a hazard to participants.

Protocol deviation is defined as an inadvertent act in which the approved IRB protocol is not followed. Examples include the accidental loss of consent form or study materials with identifiable information, or an accidental misread of a laboratory value leading to the erroneous inclusion of a participant.

Protocol violation is defined as an intentional act in which the approved IRB protocol is not followed. Examples include implementing changes to the protocol without first obtaining IRB approval, enrolling subjects after study expiration, or enrolling subjects who do not meet inclusion/exclusion criteria. A lapse in IRB approval must always be reported to the IRB as a protocol violation.

Unanticipated Problem is defined as any 1) unexpected (in terms of nature, severity, or frequency) problem or event and 2) possibly related to the participation in research, given the research procedures described in the IRB-approved protocol and the characteristics of the subject population being studied. Unanticipated problems may or may not place subjects at an increased risk of harm. An unanticipated problem may include subject complaints, protocol deviations or violations, as defined below.

For the purposes of this SOP, any of the four items identified above will be referred to as an event.

III. Procedure

Investigator Reporting Requirements and Submission

1. Any event must be reported to the IRB within 10 business days of the Principal Investigator (PI) becoming aware of the event.
2. An unanticipated study-related death must be reported to the IRB within 24 hours of the occurrence of the event.
3. The PI must submit *an IRB Adverse Event or Deviation/Violation* through InfoEd.

Review of Events

1. The IRB administrator receives the project in InfoEd and conducts an initial assessment to ensure all fields are completed and the event is adequately described.
2. The Director of the Office of Research Administration (ORA), the Research Compliance Officer (RCO), and the IRB chair review the submission and assess whether the event increases the risks to subjects or adversely affects their rights, welfare or safety, whether there is an ongoing risk of harm to participants, and how any newly identified risks may be minimized.
3. Based on the assessment, no additional action is needed, minor corrective actions are needed, or, the issue should be referred to the convened IRB. If the event is referred to the full-board, the PI will be notified in writing within 7 days of the referral.
4. If minor corrective actions are necessary, the RCO and the IRB chair work with the PI to develop an appropriate plan and determine whether any modifications to the study are needed.
5. If the issue is presented to the full-board, the IRB votes to determine whether further action is necessary. Possible actions include but are not limited to:
    a. Acknowledging the event with no further action needed.
    b. Requesting further information from the research team.
    c. Opening a non-compliance inquiry.
    d. Requiring monitoring of research procedures - including informed consent - by IRB members or ORA staff.
    e. Increasing frequency of the continuing review cycle.
    f. Requiring additional education and training for research personnel.
    g. Requiring modifications to protocol and/or informed consent process.
    h. Requiring notification of current participants of the event if the information may affect their willingness to continue participation.
    i. Suspending the study.
    j. Terminating the study.
6. If the event represents a serious risk to the participants or indicates a pattern of increasing risk to participants, the Director, RCO, and IRB chair may determine that a Non-Compliance Inquiry is appropriate without a meeting of the convened board. If an inquiry is initiated, it will follow the inquiry procedures outlined in SOP 302.
7. The RCO and chair communicates the IRB-approved actions to the PI through InfoEd within 14 business days the meeting and notifies them of any additional information or changes needed. If modifications to the study are required, the investigator submits a modification request as described in SOP 207.
8. The PI has 10 days to appeal the IRB actions in writing, if they so choose. The IRB reviews the appeal and decides whether to reject the appeal or to re-open the inquiry.
9. The RCO and Director of ORA will assist the IRB in reporting the event to external sponsors and/or regulatory agencies, if applicable to the study.

IV. Responsibilities

IRB administrators, IRB members, Investigators

V. References

45 CFR § 46.108(a)(4)
21 CFR § 56.108(b)